Height and the Survival of Prostate Cancer Patients

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Abstract

We investigated the associations between height and other anthropometric factors and the survival of 584 prostate cancer patients, initially recruited for a population-based, case-control study. During a median of 6.6 years of follow-up, 129 prostate cancer deaths and 153 deaths because of other causes were identified. After adjusting for age, cancer stage, and grade, the relative risk and 95% confident intervals for prostate cancer death were 1.0 (reference), 0.9 (0.6–1.4), 0.5 (0.3–0.9), and 0.6 (0.3–1.0) for patients whose heights were <1.75 m, 1.75–1.79 m, 1.80–1.84 m, and ≥1.85 m, respectively (*P* for trend = 0.01). Similar associations were found in subgroup analyses by cancer stage, cancer grade, age, race, and occupation-based socioeconomic status. However, height was not associated with death because of other causes. In addition, no significant associations were found between body mass index or weight and either prostate cancer death or death because of other causes. Our results suggest that greater height may be associated with better survival of prostate cancer patients.

Introduction

Prostate cancer is the most common noncutaneous cancer in men in the United States and the second leading cause of cancer death. In 2002, ~189,000 men will be diagnosed with prostate cancer, and 30,200 men will die from this disease (1). Prostate tumor stage and grade are strong predictors of patient survival (2). In the United States, African-American men with prostate cancer have poorer survival than their white counterparts (2, 3) and the difference cannot be completely explained by cancer stage and grade (4). Cases diagnosed at a younger age usually have poor prognosis (2, 3).

Epidemiological evidence relating height to prostate cancer incidence or mortality has been inconsistent, with usually a weak-positive association identified in some (5–8) but not all of the previous large cohort studies (9–12). However, to our knowledge, no study has investigated whether height is related to the survival of prostate cancer patients. In a population-based, case-control study in the United States, we reported that tallness was associated with greater risk of incident prostate cancer in Caucasians but not in African-Americans (13). Now, we followed this series of prostate cancer cases to relate height and other anthropometric variables to risk of death because of prostate cancer or other causes.

Materials and Methods

The study population was derived from two population-based registries of the SEER[2] program Georgia Center for Cancer Statistics (Clayton, Cobb, De Kalb, Fulton, and Gwinnett counties) and the Metropolitan Detroit Cancer Surveillance System (Macomb, Oakland, and Wayne counties) as part of a population-based, case-control study to investigate risk factors for this disease (13, 14). The investigation received Institutional Review Board approval from the National Cancer Institute.

All of the incident cases ages 40 years or older with a pathologically confirmed prostate cancer diagnosis between August 1, 1986 and April 30, 1989 were identified from pathology and outpatient records at hospitals covered by these registries. A random sample of cases was chosen by an age- and race-stratified sampling scheme to ensure an adequate representation of participants by age and race. The planned sampling fractions ranged from 100% for those < age 55 to 20% for white patients ages 65–74, and 17% for African-American men with prostate cancer ages 65–74 (13). Cancer cases were classified from routinely collected information by tumor stage (localized, regional, distant, and unstaged/missing) and histologic grade. The grade was classified according to the SEER system and corresponds with the Gleason score in the following way: well differentiated (Gleason 2–4), moderately differentiated (Gleason 5–7), poorly or undifferentiated (Gleason 8–10), and undetermined/missing (15). After obtaining consent, we interviewed the patients and asked about their usual adult heights in inches and weights in pounds. BMI was then calculated (kg/m^2). In addition, we also collected information on occupational history, tobacco and alcohol use, and demographics.

Of the 786 prostate cancer patients selected in the two study areas, 613 were interviewed. Reasons for nonresponse included death ($n = 36$), physician refusal ($n = 24$), patient refusal ($n = 54$), patient being too ill ($n = 9$), and others ($n = 50$). Of the 613 prostate cancer patients, 594 were linked to the SEER database for fatality follow-up, from the date of interview to the date of death or December 31, 1995, whichever came first. For decedents, information on the underlying cause of death was obtained by the registry from the death certificate and classified according to the International Classification of Diseases, 9th Revision, with code 185 for prostate cancer death. Survival status of 9 subjects could not be ascertained, and 1

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[2] The abbreviations used are: SEER, Surveillance, Epidemiology, and End Results; BMI, body mass index; SES, socioeconomic status; RR, relative risk; CI, confidence interval.

Table 1 RR (95% CI) of death because of prostate cancer or other causes by adult height

	Adult Height (m)				
	<1.75	1.75–1.79	1.80–1.84	≥1.85	*P* for trend
Person-years	935.2	846	874.3	533.4	
Median survival (years)	6.2	6.5	6.8	6.8	
Death because of prostate cancer	48	41	24	16	
Rate (/100 person-years)	5.1	4.8	2.8	3.0	
Age/stage/grade-adjusted RR	1.0	0.9 (0.6–1.4)	0.5 (0.3–0.9)	0.6 (0.3–1.0)	0.01
Fully adjusted RR[a]	1.0	0.9 (0.6–1.5)	0.6 (0.3–1.0)	0.6 (0.3–1.2)	0.05
Death because of other causes	50	42	38	23	
Rate (/100 person-years)	5.3	5.0	4.3	4.3	
Age/stage/grade-adjusted RR	1.0	0.9 (0.6–1.3)	0.9 (0.6–1.3)	0.7 (0.4–1.2)	0.2
Fully adjusted RR[a]	1.0	1.0 (0.6–1.5)	0.9 (0.6–1.5)	0.8 (0.5–1.4)	0.4

[a] Adjusted for age, prostate cancer stage and grade, race, SES, cigarette smoking, alcohol drinking, and weight.

subject had missing values on height and weight; therefore, 584 prostate cancer patients were included in the analysis. A total of 282 deaths occurred, 129 because of prostate cancer and 153 because of other causes, with a median follow-up of 6.6 years.

Parallel analyses were performed for prostate cancer death and death because of other causes, using Cox proportional hazards models to calculate RRs and 95% CIs. Linear trend was tested by using the median of each category as a continuous variable. Statistical analyses for anthropometric variables were applied to the whole cohort and then for subgroups by cancer stage (regional/distant *versus* localized), cancer grade (poorly/undifferentiated *versus* well/moderately differentiated), race (African Americans *versus* Caucasians), age (≥65 years *versus* <65 years), and occupational-based social economic status (SES: low *versus* middle/high). We adjusted for age in 5-year age groups (<55, 55–59, 60–64, 65–69, 70–74, and ≥75) and, where applicable, for cancer stage (localized, regional, distant, and unstaged/missing) and grade (well differentiated, moderately differentiated, poorly or undifferentiated, and undetermined/missing). The multivariate RRs were adjusted for age, cancer stage and grade, race, SES (low, middle, and high), cigarette smoking (never, past, and current), alcohol use (never, past, and current), and weight (kg, <70, 70.1–79.0, 79.1–88.0, >88.0). All of the significance tests were two-sided ($\alpha = 0.05$). We also examined the associations after excluding the first year of follow-up; the results were essentially unchanged.

Results

The study cohort included 264 African-American men and 320 Caucasian men with prostate cancer. Taller patients were more likely to be Caucasians, and to report greater weight and higher SES. Compared with patients <1.75 m, those ≥1.85 m tended to have more localized tumors (64.4% *versus* 57.0%) and fewer distant metastases (11.1% *versus* 19.6%); however, the trend test of this difference was not statistically significant ($P = 0.1$). Height was not associated with age, cancer grade, BMI, cigarette smoking, or alcohol drinking.

Cancer stage and grade were the strongest determinants of death because of prostate cancer. The age- and grade-adjusted RRs were 1.0 for localized tumor (reference), 2.3 for regional tumor, 7.1 for distant tumor, and 1.6 for tumor with missing stage information. Compared with well-differentiated tumor, the age- and stage-adjusted RRs were 3.1, 6.7, and 5.1, respectively, for moderately differentiated tumor, poorly/undifferentiated tumor, and tumor with undetermined/missing grade. Cancer grade and stage were not strong predictors for death because of other causes, for which age, instead, was the major determinant. Compared with patients <55 years of age, the stage- and grade-adjusted RRs for death because of other causes were 1.9, 2.8, 3.2, 4.4, and 7.3, respectively, for each 5-year age group between 55–59 years and ≥75 years. For prostate cancer death, the corresponding RRs for each age group were 1.0 (reference), 0.6, 0.8, 0.8, 0.7, and 1.6, respectively.

Greater adult height was associated with better prostate cancer survival (Table 1). The (crude) rate of prostate cancer death was 5.1/100 person-years among the shortest patients and only 3.0/100 person-years among the tallest; the RR was 0.6 (P for trend = 0.01) after adjustment for age, stage, and grade. Additional adjustment for race, SES, smoking, drinking, and weight did not change the estimates. The improved survival differential for taller men was found consistently within subgroups of other prostate cancer survival determinants (Table 2). For death because of other causes, taller men also tended to have decreased risk; however, the trend test was not statistically significant (Table 1; P for trend = 0.2). Neither BMI nor adult weight was associated with the survival of prostate cancer patients. For example, compared with BMI <23.0 kg/m^2, after adjusting for age, cancer stage, and grade, the RRs for BMI ≥27.0 kg/m^2 was 1.2 for prostate cancer death (P for trend = 0.8) and 0.9 for death because of other causes (P for trend = 0.4).

Discussion

Tallness has been hypothesized to be associated with greater risk of developing prostate cancer because it could serve as an indicator of higher energy intake, and greater exposures to testosterone and growth hormones in childhood and adolescence (7). However, previous epidemiological evidence regarding this association has not been consistent (5–7, 9–11). Large cohort studies of height and prostate cancer mortality also generated inconsistent results. A statistically significant, albeit weak, positive association was identified in a Swedish cohort and the older cohort of a United States investigation (5, 8), but not in three other Western cohorts (8, 12, 16).

Previous studies did not provide direct data on height and the survival of prostate cancer patients. In this study, height was inversely associated with death because of prostate cancer among prostate cancer patients. Potential confounding from measured covariates is likely to be small as shown in the multivariate and subgroup analyses. To explore the possibility that the inverse association was driven by the early-life nutritional status of patients, we examined the association according to age, race, and SES. We assumed that the associations might be stronger among older patients, African-Americans, or patients with lower SES, because their heights were more likely

Table 2 RR[a] (95% CI) of death because of prostate cancer by adult height in subgroup analyses

	Height (m)	Death/person-years[b]	Rate (/100 person-years)	RR (95% CI)
Cancer stage				
Regional/distant	<1.80	51/360.3	14.2	1.0
	≥1.80	25/314.5	7.9	0.5 (0.3–0.9)
Local	<1.80	29/1,153.3	2.5	1.0
	≥1.80	9/948.3	0.9	0.4 (0.2–0.8)
Cancer grade				
Poorly/undifferentiated	<1.80	44/282.6	15.6	1.0
	≥1.80	19/269.1	7.1	0.4 (0.3–0.8)
Well/moderately differentiated	<1.80	37/1348.5	2.7	1.0
	≥1.80	17/1051.4	1.6	0.7 (0.4–1.4)
Age				
>65 years	<1.80	45/879.6	5.1	1.0
	≥1.80	20/563.5	3.5	0.5 (0.3–0.9)
≤65 years	<1.80	44/901.6	4.9	1.0
	≥1.80	20/844.2	2.4	0.6 (0.3–1.0)
Race				
African Americans	<1.80	52/797.1	6.5	1.0
	≥1.80	15/522.1	2.9	0.5 (0.3–0.9)
Caucasians	<1.80	37/984.1	3.8	1.0
	≥1.80	25/885.6	2.8	0.7 (0.4–1.1)
SES				
Low	<1.80	51/844.0	6.0	1.0
	≥1.80	19/596.8	3.2	0.5 (0.3–0.9)
Middle/high	<1.80	38/936.4	4.1	1.0
	≥1.80	21/810.8	2.6	0.5 (0.3–0.9)

[a] Age, cancer stage, and grade were adjusted when applicable.
[b] Numbers may not add up to total because of missing values.

to be affected by early-life nutritional factors compared with the rest of the patients. We did not observe substantial differences across these factors. Similarly, the inverse association between height and risk of prostate cancer death is not likely to be explained by biases. We asked prostate cancer patients to recall their usual adult height to avoid the effect of height loss because of aging or medical conditions; previous studies showed that height was usually accurately recalled (17). Moreover, height is not likely to be related to the ascertainment of deaths during the follow-up. Finally, greater height was associated slightly with lower risk of death from other causes in this study, auguring against competing risk of other deaths as a potential explanation for the observed association.

The underlying mechanism for the observed association is not clear. Tumor cell metastasis is a major determinant of cancer patient survival, and bone is the most common metastasis site in prostate cancer (18). It is possible that tallness is associated with some characteristics of bone quality and a hormonal milieu that may help to slow down the progress of prostate cancer cell metastasis to bone. Our observation of decreased prostate cancer mortality with greater height, among Caucasians and African-Americans, appears to contradict our earlier observations (13) of increased incidence with greater height among Caucasians (although we found no impact of height on prostate cancer incidence in African-Americans). Findings on height and prostate cancer risk remain uncertain (5–12), and more detailed incidence and mortality follow-up studies are needed to put these possible discrepancies in context.

Interpretation of our results should consider potential limitations of this study. Treatment information was not available in this study, and bias could be introduced if height was associated with treatment choice. However, it is unlikely that height has an appreciable association with treatment after adjusting for cancer stage and grade, age, race, and SES. Secondly, we did not have data on prostate-specific antigen screening, which may preferably identify slower-growing tumors (19). However, the inverse association between height and prostate cancer death was observed irrespective of cancer stage and grade, and height might not relate to prostate-specific antigen screening in the late 1980s.

Our study suggests that tallness may be associated with lower risk of prostate cancer death among prostate cancer patients. However, this preliminary result needs to be confirmed in other studies, and the underlying mechanism needs to be identified.

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